PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Merrill A. Biel	
Serial No.: 10/026,198	Group Art Unit: 3735
Filed: December 21, 2001	Examiner: D. Shay
For: PHOTODYNAMIC CELLULAR AND ACELLULAR ORGANISM ERADICATION UTILIZING A PHOTOSENSITIVE MATERIAL AND BENZALKONIUM CHLORIDE	Atty. Dkt. No.: 22,272-22

APPEAL BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-01450

This brief is filed in response to the Notification of Non-Compliant Appeal Brief mailed August 19, 2008, regarding the above-captioned application.

I. Real Party in Interest

The real party in interest is Merrill A. Biel.

II. **Related Appeals and Interferences**

An appeal associated with US Ser. No. 09/792,578 may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal. No decision has been rendered by a court or the Board in that proceeding.

III. Status of Claims

Claims 1-52 were filed with the application. Claims 8, 17, 21, and 35-39 have been canceled. Thus, claims 1-7, 9-16, 18-20, 22-34 and 40-52 are pending, stand rejected, and are appealed herein. A copy of the pending claims is attached.

IV. Status of Amendments

An amendment dated January 30, 2005 was submitted and not entered. The listing of claims below reflects the claims prior to the proposed amendment of January 30, 2005.

V. Summary of Claimed Subject Matter

The present invention involves a method of eradicating pathogenic cells, such as cancer cells, microbes, spores and fungi utilizing a photodynamic therapy. In particular, the present invention shows that such pathogenic cells may be eradicated by a photodynamic modality utilizing a photosensitive material and a particular surface acting agent, benzalkonium chloride. Additional aspects of the invention include the utilization of such a method within an air filtration / decontamination device.

A concise explanation of the claims and reference to the specification by page and line number, and to the drawings, follows.

Claim 1 is directed to a method of photodynamic disruption of cellular organisms comprising the steps of applying a surface acting agent containing benzalkonium chloride at a concentration of between 0.001% to 1.0% to a cell membrane of a cellular organism, said surface acting agent disorienting a cell membrane so that said cell membrane no longer functions as an effective osmotic barrier; passing a photosensitive material through the disoriented membrane and into the cell interior; and applying light to the cellular organism to cause a cellular disruption of the cellular organism. (p. 23, lns. 8-10; p. 22, ln. 18, p. 15, ln. 31; p. 16, lns 1 – 3; p. 15 lns. 10 – 24, FIGS. 2 – 6.)

Claims 2 and 16 are directed to a method of organism disruption wherein the surface acting agent and the photosensitive material are provided in a combined solution. (p. 17, ln. 15.)

Claim 3 is directed to a method of cellular organism disruption of claim 2 wherein the combined solution is provided in proximity to the cellular organism via a topical application. (p. 17, ln. 15.)

Claims 4, 18, 33 and 40 are directed to methods wherein the step of applying the surface acting agent and the step of passing the photosensitive material is performed on cellular

organisms located on a surface of a medical prosthesis. (p. 17, lns. 20-31, p. 18, lns. 1-8, p. 21, lns. 3-29, p. 22, lns. 1 – 30, FIGS. 4 and 5.)

Claims 5 and 20 are directed to methods wherein the photosensitive material is monomeric, dimeric, or polymeric. (p. 27, ln. 20.)

Claims 6 and 19 are directed to methods wherein the organism is associated with one of the following: a sterilization procedure, a biofilm eradication procedure, a treatment of an infection at a tissue site, eradication of cancer cells, and an air filtration/decontamination process. (p. 23, lns. 11-20, p. 24, lns. 1 – 12, p. 24, lns. 20-29, p. 25, lns. 1-30, p. 26, lns. 3-23; FIGS. 2-6.)

Claims 7 and 30 are directed to a method wherein the organism is a microbe, a spore, a fungus, or a cancer cell. (p. 18, ln. 28; p. 10, ln. 1 – 5.)

Claims 9 and 22 are directed to methods of organism disruption wherein the surface acting agent contains benzalkonium chloride provided in a concentration range of between 0.005% to 0.05%. (p. 32, ln. 10.)

Claims 10 and 26 are directed to methods of organism disruption wherein the step of applying the surface acting agent precedes the step of passing the photosensitive material by between 1 to 30 minutes. (p. 17, ln. 19.)

Claims 11 and 24 are directed to methods of organism disruption wherein the step of applying light to the cellular organism occurs for a period of between 5 seconds to 1 hour and results in cellular organism death. (p. 16, ln. 23.)

Claims 12 and 29 are directed to methods of organism disruption wherein the step of applying a light includes a light wavelength ranging from 450 nm to 780 nm and a light dosage

ranging from 10 J/cm^2 to 100 J/cm^2 and a light dosage rate ranging from 50 mw/cm^2 to 250 mw/cm^2. (p. 9, lns. 18-22.)

Claims 13 and 27 are directed to methods of organism disruption wherein the step of applying the surface acting agent includes providing more than one of a plurality of different surface acting agents. (p. 18, lns. 15-22.)

Claims 14 and 28 are directed to a method of organism disruption wherein the step of passing the photosensitive material includes providing more than one of a plurality of different photosensitive materials. (p. 18, ln. 22.)

Claim 15 is directed to a method of photodynamic disruption of organisms comprising the steps of topically applying a surface acting agent containing benzalkonium chloride at a concentration of between 0.001% to 1.0% to a cell site with an organism, said surface acting agent disorienting a membrane of the organism so that said membrane no longer functions as an effective osmotic barrier; passing a photosensitive material in association with the organism, said photosensitive material being accumulated within the membrane of the organism; and applying light to the organism to cause a disruption of the organism. (p. 22, lns. 16-30.)

Claim 23 is directed to a method of organism disruption wherein the step of applying light results in organism destruction. (FIGS. 2 – 4.)

Claim 25 is directed to a method of organism disruption wherein the step of applying light occurs for a period of between 2 to 20 minutes. (p. 30, ln. 16.)

Claim 31 is directed to a method of photodynamic disruption of cells comprising the steps of: identifying an area of cell activity; applying a concentration including a combination of a benzalkonium chloride compound at a concentration of between 0.001% to 1.0% and a photosensitive material to the area of cell activity, said benzalkonium chloride compound

disorienting a cell membrane so that said membrane no longer functions as an effective osmotic barrier, and so that said photosensitive material is able to pass through the disoriented cell membrane; and exposing the area of cell activity to light having a light wavelength, a light dosage and a light dosage rate to cause photodynamic cellular disruption. (p. 22, lns. 16-30.)

Claim 34 is directed to a method of photodynamic disruption of cells wherein the step of identifying an area of cell activity includes identifying an air filtration/decontamination device, and the step of providing the concentration includes an application of the concentration to a cell site within the device. (p. 25, lines 23-29, p. 26, lns. 1-23, FIG. 6.)

Claim 41 is directed to the method of claim 40 wherein the surfactant is benzalkonium chloride provided in at a concentration of between 0.001% to 1.0%. (p. 23, ln. 9.)

Claim 42 is directed to the method of claim 41 wherein the step of applying the photosensitive material and the surfactant is via an impregnation of compounds upon a surface of the prosthesis. (p. 10, lns. 19-29, p. 24, ln. 4.)

Claim 43 is directed to the method of claim 41 wherein the step of illuminating the biofilm layer is achieved by an internal illumination of the prosthesis. (p. 24, lns. 1-12, FIG. 5.)

Claim 44 is directed to the method of claim 41 wherein the step of illuminating the biofilm layer is achieved by an external light source illuminating the biofilm layer. (p. 24, lns. 1-12, FIG. 5.)

Claims 45 and 49 are directed to a method of photodynamic eradication of organisms within a biofilm layer of a medical apparatus, said method comprising the steps of: providing a photosensitive material and a surfactant to a surface of the medical apparatus supporting a biofilm layer; accumulating photosensitive material within the organisms comprising the biofilm; allowing the surfactant to disrupt membranes of the organisms within the biofilm; waiting a

period of time until the photosensitive material accumulates within organisms; providing a source of light illumination having predetermined light characteristics; and illuminating the biofilm layer of the endotracheal tube with the light source to achieve a photodynamic eradication of organisms within the biofilm layer. (p. 24, lns. 10-29, p. 25, lns. 1-6, FIG. 5.)

Claims 46 and 50 are directed to a method wherein the surfactant is benzalkonium chloride provided at a concentration of between 0.001% to 1.0%. (p. 23, ln. 9.)

Claim 47 and 51 are directed to a method wherein the step of providing the photosensitive material and the surfactant is via an impregnation of compounds upon a surface of the medical apparatus. (p. 10, lns. 24-29, p. 24, ln. 4.)

Claims 48 and 52 are directed to a method wherein the step of illuminating the biofilm layer is achieved by an internal illumination of the medical apparatus. (p. 24, lns. 1-12.)

VI. Grounds of Rejection to be Reviewed on Appeal

1. Are claims 1-3, 5-7, 9, 11, 15, 16, 19, 20, 22-25 and 30-32 rejected under 35 U.S.C. §102(b) as being anticipated by Vogel et al?

2. Are claims 1-4, 5-7, 9, 11, 15, 16, 18-20, 22-25, 30-34 and 40-52 rejected under 35 U.S.C. §103(a) as being unpatentable over Wilk et al. ('020) in combination with Wilk et al. ('675) and Vogel et al?

3. Are claims 1, 5, 10-15, 20 and 26-29 rejected under 35 U.S.C. §103(a) as being unpatentable over Vogel et al. in combination with Nitzan et al.?

VII. Argument

Grouping of the Claims

a. Regarding the §102(b) rejection based on Vogel et al, claims 1, 6, 9, 11, 19, 22, 24, 25 and 26 do not stand or fall together.

b. Regarding the 103(a) rejection based on Wilk '020 in combination with Wilk '675 and Vogel, claims 1, 6, 19, 34, 42, 47 and 51 do not stand or fall together.

c. Regarding the 103(a) rejection based on Vogel in combination with Nitzan, claims 1, 10 and 26 do not stand or fall together.

Summary of the Arguments

a. Vogel does not disclose the mechanism of passing photosensitive material into the cell interior, i.e., by applying benzalkonium chloride to compromise a cell membrane so as to permit the photosensitive material to diffuse into the cell interior. Vogel does not disclose a topical application, surface release, inhalation, or intravenous or subcutaneous injection of benzalkonium chloride wherein the concentration of benzalkonium chloride is within the 0.001% to 1% range at the cell site. An intravenous administration of Vogel would not result in a benzalkonium chloride concentration at a cell site within this range as the intravenously administered solution would be instantly and effectively diluted within the approximately 5 liters volume of patient's blood. Regarding claim 1, Vogel does not disclose the step of applying a surface acting agent containing benzalkonium chloride at a concentration of between 0.001% to 1.0% to a cell membrane of a cellular organism. Regarding claims 6 and 19, Vogel does not disclose an air filtration / decontamination process.

b. It is submitted that this proposed combination of Wilk et al ('675), Wilk et al ('020) and Vogel is flawed as there would be no motivation to replace the IV solution of Vogel with the saline solution in Wilk ('675) or the sterilizing solution of Wilk ('020). Wilk et al. ('020) discloses the use of a saline solution flush during a sterilization process. However, Wilk ('020) does not teach the use of a "sterilizing solution". Saline solution is not a "sterilizing solution" to one of ordinary skill in the art. The saline solution of Wilk et al. ('020) is provided to ensure electrical conductivity of the solution. As saline solution has no antimicrobial properties, such a solution is not a "sterilizing solution" as suggested by the Examiner. Wilk et al ('675) discloses the use of a "sterilizing solution" during a sterilizing process utilizing a combination of heat and radiation. Wilk '675 does not disclose or suggest the use of photodynamic activity during a sterilization process. As a result, there is not suggestion or motivation to combine these references. Regarding claims 6, 19 and 34, Wilk '020, Wilk '675 and Vogel do not disclose an air filtration /decontamination process or apparatus for performing such a process. Regarding claims 42, 47 and 51, Wilk '020, Wilk '675 and Vogel do not disclose the step of applying the photosensitive material and the surfactant via impregnation of these compounds on the surface of the prosthesis or tube or catheter. The generally accepted definition of "impregnation" is the process of saturating something with a substance. Neither Vogel nor Wilk '020 or Wilk '675 disclose or suggest surface impregnation of photosensitive material and surfactant on the surface of a prosthesis, tube or catheter.

c. Nitzan teaches away from the concept of using photosensitizers and a surfactant such as benzalkonium chloride to increase the cell membrane permeability and allow the photosensitizer to enter the cell by diffusion as is disclosed in the present invention. Nitzan emphasizes the importance of binding the photosensitive material to the outer cell membrane wall and that the

nature of the totality of teaching of the reference would direct one of ordinary skill in the art toward the use of particular surfactants which would improve the binding of photosensitive material to the outer cell wall, and away from the use of benzalkonium chloride to breach the cytoplasmic cell membrane and allow the photosensitive material into the cell interior prior to photodynamic activation. Given the distinction between the functions of the surfactant of Nitzan and benzalkonium chloride of the present invention, there would be no motivation to substitute or add benzalkonium chloride with the PMNP of Nitzan. While benzalkonium chloride may "inhibit bacterial and fungal contamination of the solution" as suggested by the Examiner, that alone would not motivate one to substitute benzalkonium chloride for the solution of Nitzan as the function of the surfactant is fundamentally different between Nitzan and the present invention, i.e., to facilitate binding of photosensitive material to the outer cell wall (Nitzan) and to facilitate breaching of the cytoplasmic cell membrane so as to allow photosensitive material to accumulate within the cell interior prior to photodynamic activation (present invention). A proposed modification of Nitzan to substitute PMNP with benzalkonium chloride would not be obvious as such a modification would change the principle of operation of the prior art invention being modified. See, MPEP §2143.01, citing In re Ratti 123 USPQ 349.

Claims 10 and 26 are directed to the step of applying the surface acting agent prior to the step of applying and passing the photosensitive material through a compromised cell membrane. It is submitted that this proposed combination of Vogel and Nitzan, even if proper, would fail to yield the invention of claim 10. Vogel purportedly discloses only a combined solution of photosensitive material and surfactant in a topical preparation and intravenous solutions. Col. 11, lines 36 – 50. A combined solution is the antithesis of separate administrations of the surface acting agent and photosensitive material.

Arguments

A. Standard of Review

Findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the Administrative Procedure Act, 5 U.S.C. §706(A), (E), 1994. *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999). Moreover, the Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by "substantial evidence" within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *In re Gartside*, the Federal Circuit stated that "the 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Id.* at 1312. Accordingly, it necessarily follows that an Examiner's position on Appeal must be supported by "substantial evidence" within the record in order to be upheld by the Board of Patent Appeals and Interferences.

B. Rejection Under 35 U.S.C. §102(b) Over Vogel et al.

Claims 1-3, 5-7, 9, 11, 15, 16, 19, 20, 22-25 and 30-32 were rejected under 35 U.S.C. §102(b) as being anticipated by Vogel et al.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. M.P.E.P. §2131. Anticipation can be found only if a reference shows exactly what is claimed. *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). Anticipation requires identity of the claimed process and a process of the prior art; the claimed process, including each step thereof, must be described or embodied in a single reference. *Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc.*, 45 F.3d 1550, 22 USPQ2d 1496 (Fed. Cir. 1995).

Vogel et al. is an improper 102 reference of the claims as amended.

Vogel et al. discloses an intravenous solution of photoactivatable porphycene dyes and additional solvents and adjuvants. Col. 11., Lines 45 – 47. When the intravenous solution is be dispensed from multiple dose containers, antimicrobial agents in bacteriostatic or fungistatic concentrations must be added. Col. 12, Lines 41 – 43. Among the compounds and concentrations used as an antimicrobial agent is benzalkonium chloride (0.01%). Col. 12, Line 46. Vogel et al. discloses the use of benzalkonium chloride with the porphycene compound, but only in the context of the known use of benzalkonium chloride, that of a bactericidal agent. Benzalkonium chloride is used to prevent bacterial or fungal growth in the multiple dose container which may occur as a result of repeated extraction of porphycene compound from the multiple dose container. Vogel does not disclose the method of use of benzalkonium chloride to disrupt the membrane of a cell thereby allowing photosensitive agents to enter the cell. That Vogel et al. uses benzalkonium chloride as an antimicrobial agent is not unexpected, as benzalkonium chloride is a well known medical disinfectant.

The anticipation rejection based on Vogel et al. is improper for the following reasons:

– Vogel does not disclose the mechanism of passing photosensitive material into the cell interior, i.e., by applying benzalkonium chloride to compromise a cell membrane so as to permit the photosensitive material to diffuse into the cell interior, and

– Vogel does not disclose a topical application, surface release, inhalation, or intravenous or subcutaneous injection of benzalkonium chloride wherein the concentration of benzalkonium chloride is within the 0.001% to 1% range at the cell site. An intravenous administration of Vogel would not result in a benzalkonium chloride concentration at a cell site within this range as the intravenously administered solution would be instantly and effectively diluted within the approximately 5 liters volume of patient's blood.

Additional arguments regarding specific claims include:

Claim 1: Vogel does not disclose the step of applying a surface acting agent containing benzalkonium chloride at a concentration of between 0.001% to 1.0% to a cell membrane of a cellular organism.

Claim 3: Vogel does not teach or suggest a topical application of benzalkonium chloride wherein the concentration of benzalkonium chloride is within the 0.001% to 1% range at the cell site.

Claim 9: Vogel does not disclose the step of applying a surface acting agent containing benzalkonium chloride at a concentration of between 0.005% to 0.05% to a cell membrane of a cellular organism.

Claim 11: Vogel does not disclose the steps of applying a surface acting agent containing benzalkonium chloride at a concentration of between 0.005% to 0.05% to a cell membrane of a cellular organism and applying light to the cellular organism for a period of between 5 sections to 1 hour.

Claims 15-17 and 19-25 and 30: Vogel does not disclose the step of topically applying a surface acting agent containing benzalkonium chloride at a concentration of between 0.001% to 1.0% to a cell site with an organism.

Claim 22: Vogel does not disclose the step of topically applying a surface acting agent containing benzalkonium chloride at a concentration of between 0.005% to 0.5% to a cell site with an organism.

Claims 31 and 32: Vogel does not disclose the step of applying a concentration including a combination of a benzalkonium chloride compound at a concentration of between 0.001% to 1.0% and a photosensitive material to the area of cell.

Applicant challenges the Examiner's statement:

> "Thus even assuming Vogel et al were completely ignorant of the effect of benzalkonium chloride contemplated by the applicant, thus [sic] effect, and thus the claimed disorienting, passing, and disruption would still inherently occur in the method of Vogel et al."

Vogel et al does not inherently disclose the claimed disorienting, passing, and disruption at the cell site. Vogel et al discloses an IV administration of a dye solution containing trace amounts of benzalkonium chloride as an antimicrobial agent. One of ordinary skill in the art would readily appreciate that an IV solution is quickly and effectively diluted into the patient's blood volume. As a result, Vogel does not disclose the application of benzalkonium chloride at the claimed concentrations to a cell site prior to photodynamic illumination at that cell site. Inherency may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a give set of circumstances is not sufficient. *In re Robertson*, 49 USPQ2d 1949 (Fed. Cir. 1999).

In light of the arguments above, it is suggested that claims 1-3, 5-7, 9, 11, 15, 16, 19, 20, 22-25, and 30-32 are not anticipated by Vogel et al.

C. Rejection Under 35 U.S.C. §103

i. 35 U.S.C. §103(a): Wilk '020 in combination with Wilk '675 and Vogel et al.

Claims 1-4, 5-7, 9, 11, 15, 16, 18-20, 22-25, 30-34 and 40-52 were rejected under 35 U.S.C. §103(a) as being unpatentable over Wilk et al. ('020) in combination with Wilk et al. ('675) and Vogel et al.

It is submitted that this proposed combination of Wilk et al. ('675), Wilk et al. ('020) and Vogel et al. is flawed as there would be no motivation to replace the IV solution of Vogel with the saline solution in Wilk ('675) or the sterilizing solution of Wilk ('020).

Wilk et al. ('020) discloses the use of a saline solution flush during a sterilization process. However, Wilk ('020) does not teach the use of a "sterilizing solution". Saline solution is not a "sterilizing solution" to one of ordinary skill in the art. The saline solution of Wilk et al. ('020) is provided to ensure electrical conductivity of the solution. As saline solution has no antimicrobial properties, such a solution is not a "sterilizing solution" as suggested by the Examiner.

Wilk et al ('675) discloses the use of a "sterilizing solution" during a sterilizing process utilizing a combination of heat and radiation. Wilk '675 does not disclose or suggest the use of photodynamic activity during a sterilization process. As a result, there is not suggestion or motivation to combine these references.

The Examiner is simply engaging in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps, an activity the Federal Circuit has repeatedly indicated as improper. *In re Gorman*, 933 F.2d 982, 19 USPQ2d 1885 (Fed. Cir. 1991). There must be some reason for the combination other than the hindsight obtained from the invention itself. *Interconnect Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 228 USPQ 90 (Fed. Cir. 1985). The Examiner has not established a prima facie case of obviousness by failing to provide the motivation or reasoning as to why the combination of references is proper.

Furthermore, as additional support to the nonobviousness of the present invention, we have submitted a product listing sheet and a published article on benzalkonium chloride. Both publications state that benzalkonium chloride is unacceptable sterilant of medical equipment. Similarly, data in FIGS. 2 and 3 suggest that benzalkonium chloride is an ineffective sterilant. It is only through the novel method employed in the present invention that benzalkonium chloride

can be effectively used in a sterilization process for medical equipment. An unexpected result of the present invention is that a photodynamic therapy using benzalkonium chloride is effective against a broad spectrum of organisms including gram positive and gram negative bacteria, funguses, viruses, spores and cancer cells.

The present invention as currently claimed is not made obvious by the combination of Wilk '020, Wilk '675 and Vogel. Consequently, we respectfully request that the rejections based thereon be withdrawn.

Claim 34 is separately patentable:

Claim 34 is directed to air filtration / decontamination process. The specification discloses an air filtration / decontamination device suitable for heating-ventilating-air conditioning (HVAC) use within a building or other structure in FIG. 6 and pages 25 – 26 of the specification. In the illustrated embodiment, the air filtration / decontamination device includes a filter element, a solution bath, and a light source. Contaminated air is directed through the device to filter and decontaminate the air.

Vogel does not disclose or suggest an air filtration or decontamination device or related method of use. The rejection of claim 34 based on Vogel et al in combination with Wilk '020 and Wilk '675 is in error.

Claims 42, 47 and 51 are separately patentable:

It is submitted that this proposed combination of Wilk et al ('675), Wilk et al ('020) and Vogel, even if proper, would fail to teach or suggest the invention of claims 42, 47 and 51. Claims 42, 47 and 51 includes the step of applying the photosensitive material and the surfactant via impregnation of these compounds on the surface of the prosthesis or tube or catheter. The generally accepted definition of "impregnation" is the process of saturating something with a

substance. Neither Vogel nor Wilk '020 or Wilk '675 disclose or suggest surface impregnation of photosensitive material and surfactant on a surface of a prosthesis, tube or catheter. Reconsideration of this rejection is requested.

ii. 35 U.S.C. §103(a): Vogel et al. in combination with Nitzan et al.

Claims 1, 5, 10-15, 20 and 26-29 were rejected under 35 U.S.C. §103(a) as being unpatentable over Vogel et al. in combination with Nitzan et al. The Examiner stated:

> "Vogel et al teach a method of eradicating acellular or cellular organisms as claimed but does not teach adding the surface acting agent prior to the photosensitive material, or a plurality of photosensitive or surface acting agents or the light dosage rate."

It is respectfully submitted that Vogel does not teach a method as claimed except for the adding the surface acting agent prior to the photosensitive material, or a plurality of photosensitive or surface acting agents or the light dose rate. Vogel does not teach or suggest the mechanism of introducing photosensitive material into a cell interior by application of benzalkonium chloride to compromise a cell membrane.

The Examiner further stated:

> "Nitzan et al teach a method of photosensitizing cells using a photosensitive surfactant mixture which will perform as claimed (The PMNP, which is made from Polymyxin B sulfate, will retain some of amount of Polymyxin B sulfate therein, and thus is considered a mixture of a plurality of surfactants) except for the specific time period between the addition of the two agents and the use of benzalkonium chloride." Paper 7, Page 3.

Nitzan et al does not disclose, teach, or suggest the method as claimed except for the specific time period between the addition of the two agents and the use of benzalkonium. Nitzan teaches the use of polycationic agent polymyxin nonapeptide (PMNP) and the photosensitizer deuteroporphyrin (DP) to eradicate the gram negative bacteria E Coli and Pseudomonas

aerugenosa. Nitzan uses the PMNP to bind the PMNP-DP complex to the outer cell wall, much as a membrane specific antibody would. Neither PMNP or the PMNP-DP complex cause a disruption of the cytoplasmic cell membrane (pp 94 1st column). Unlike the present invention, Nitzan teaches the use of a surfactant to assist in the binding of the photosensitizer to the cell membrane exterior, i.e. the outer cell wall. Nitzan does not disclose or suggest passing a photosensitizer through a surfactant-compromised cytoplasmic cell membrane.

There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the art would make the combination to achieve the subject matter of the present claims. *See*, Symbol Technologies, Inc. v. Opticon Inc., 935 F.2d 1569, 19 USPQ2d 1241 (Fed. Cir. 1991). Since no such reason, suggestion or motivation exists, the pending claims are not obvious in view of the known prior art.

Vogel discloses the use of surfactants with porphycene in the formulation of a topically applied compounds. The surfactants are used to improving the viscosity of the gel. Vogel does not disclose the use of benzalkonium chloride to improve the viscosity of a gel. It would not have been obvious to one of ordinary skill in the art to employ benzalkonium chloride in the method of Nitzan et al, since Vogel does not state that benzalkonium chloride may be added to improve gel properties.

Nitzan clearly does not disclose the method of compromising the cell membrane (the inner cytoplasmic membrane), allowing the photosensitive material to pass into the cell interior, and then activating the photosensitive material within the cell interior to cause cell disruption. At most, Nitzan discloses a compromised outer wall membrane as a result of photodynamic activation of photosensitive material bound to the outer cell membrane exterior. Only after cell lysis is the photosensitive material of Nitzan capable of being passed through the compromised

cytoplasmic cell membrane or membrane remnants. Again, in comparison the present invention is directed to the steps of compromising a cytoplasmic cell membrane with benzalkonium chloride, allowing the photosensitive material to pass into the cell membrane, and then activating the photodynamic process via light activation resulting in the lysis of the cell membrane.

Nitzan teaches away from the concept of using photosensitizers and a surfactant such as benzalkonium chloride to increase the cell membrane permeability and allow the photosensitizer to enter the cell by diffusion as is disclosed in the present invention. This statement is supported by the fact that Nitzan emphasizes the importance of binding the photosensitive material to the outer cell membrane wall and that the nature of the totality of teaching of the reference (See In re Guley 31 USPQ 2d 1130) would direct one of ordinary skill in the art toward the use of particular surfactants which would improve the binding of photosensitive material to the outer cell wall, and away from the use of benzalkonium chloride to breach the cytoplasmic cell membrane and allow the photosensitive material into the cell interior prior to photodynamic activation. Given the distinction between the functions of the surfactant of Nitzan and benzalkonium chloride of the present invention, there would be no motivation to substitute or add benzalkonium chloride with the PMNP of Nitzan. While benzalkonium chloride may "inhibit bacterial and fungal contamination of the solution" as suggested by the Examiner, that alone would not motivate one to substitute benzalkonium chloride for the solution of Nitzan as the function of the surfactant is fundamentally different between Nitzan and the present invention, i.e., to facilitate binding of photosensitive material to the outer cell wall (Nitzan) and to facilitate breaching of the cytoplasmic cell membrane so as to allow photosensitive material to accumulate within the cell interior prior to photodynamic activation (present invention). A proposed modification of Nitzan to substitute PMNP with benzalkonium chloride would not be

obvious as such a modification would change the principle of operation of the prior art invention being modified. See, MPEP §2143.01, citing In re Ratti 123 USPQ 349.

As such, the claims as amended are not made obvious in light of the cited references. Consequently, we respectfully request that the rejection based on Vogel and Nitzan be withdrawn.

Claim 10, 26 are separately patentable:

The examiner is merely relying on impermissible hindsight for the rejection of claims 10 and 26. As a result, this rejection is in error.

D. Conclusion

In light of the foregoing, appellants respectfully submit that all pending claims patentable. Therefore, it is respectfully requested that the Board reverse each of the pending rejections.

Respectfully submitted,

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Date: Sept. 17, 2008

CLAIMS APPENDIX

1. (previously presented) A method of photodynamic disruption of cellular organisms comprising:

applying a surface acting agent containing benzalkonium chloride at a concentration of between 0.001% to 1.0% to a cell membrane of a cellular organism, said surface acting agent disorienting a cell membrane so that said cell membrane no longer functions as an effective osmotic barrier;

passing a photosensitive material through the disoriented membrane and into the cell interior; and

applying light to the cellular organism to cause a cellular disruption of the cellular organism.

2. (previously presented) The method of cellular organism disruption of claim 1 wherein the surface acting agent and the photosensitive material are provided in a combined solution.

3. (previously presented) The method of cellular organism disruption of claim 2 wherein the combined solution is provided in proximity to the cellular organism via a topical application.

4. (previously presented) The method of cellular organism disruption of claim 1 wherein the step of applying the surface acting agent and the step of passing the photosensitive material is performed on cellular organisms located on a surface of a medical prosthesis.

5. (original) The method of cellular organism disruption of claim 1 wherein the photosensitive material is monomeric, dimeric, or polymeric.

6. (original) The method of cellular organism disruption of claim 1 wherein the cellular organism is associated with one of the following: a sterilization procedure, a biofilm eradication procedure, a treatment of an infection at a tissue site, eradication of cancer cells, and an air filtration/decontamination process.

7. (original) The method of cellular organism disruption of claim 1 wherein the cellular organism is a microbe, a spore, a fungus, or a cancer cell.

8. (canceled)

9. (original) The method of cellular organism disruption of claim 1 wherein the surface acting agent contains benzalkonium chloride provided in a concentration range of between 0.005% to 0.05%.

10. (previously presented) The method of cellular organism disruption of claim 1 wherein the step of applying the surface acting agent precedes the step of passing the photosensitive material by between 1 to 30 minutes.

11. (previously presented) The method of cellular organism disruption of claim 1 wherein the step of applying light to the cellular organism occurs for a period of between 5 seconds to 1 hour and results in cellular organism death.

12. (original) The method of cellular organism disruption of claim 1 wherein the step of applying a light includes a light wavelength ranging from 450 nm to 780 nm and a light dosage ranging from 10 J/cm^2 to 100 J/cm^2 and a light dosage rate ranging from 50 mw/cm^2 to 250 mw/cm^2.

13. (previously presented) The method of cellular organism disruption of claim 1 wherein the step of applying the surface acting agent includes providing more than one of a plurality of different surface acting agents.

14. (previously presented) The method of cellular organism disruption of claim 13 wherein the step of passing the photosensitive material includes providing more than one of a plurality of different photosensitive materials.

15. (previously presented) A method of photodynamic disruption of organisms comprising:

topically applying a surface acting agent containing benzalkonium chloride at a concentration of between 0.001% to 1.0% to a cell site with an organism, said surface acting agent disorienting a membrane of the organism so that said membrane no longer functions as an effective osmotic barrier;

passing a photosensitive material in association with the organism, said photosensitive material being accumulated within the membrane of the organism; and

applying light to the organism to cause a disruption of the organism.

16. (previously presented) The method of organism disruption of claim 15 wherein the surface acting agent and the photosensitive material are in a combined solution.

17. (canceled)

18. (previously presented) The method of organism disruption of claim 15 wherein the step of applying the surface acting agent and the step of passing the photosensitive material occurs on a surface of a medical prosthesis.

19. (previously presented) The method of organism disruption of claim 15 wherein the organism is associated with one of the following: a sterilization procedure, a biofilm eradication procedure, an air filtration / decontamination device, and a treatment of an infection at a tissue site.

20. (previously presented) The method of organism disruption of claim 15 wherein the photosensitizing agent is monomeric, dimeric, or polymeric.

21. (canceled)

22. (previously presented) The method of organism disruption of claim 15 wherein the benzalkonium chloride is provided in a concentration range of between 0.005% to 0.5%.

23. (previously presented) The method of organism disruption of claim 15 wherein the step of applying light results in organism destruction.

24. (previously presented) The method of organism disruption of claim 15 wherein the step of applying light occurs for a period of between 5 seconds to 1 hour and results in organism death.

25. (previously presented) The method of organism disruption of claim 24 wherein the step of applying light occurs for a period of between 2 to 20 minutes.

26. (previously presented) The method of acellular disruption of claim 15 wherein the step of applying the surface acting agent precedes the step of providing the photosensitive material by between 1 to 30 minutes.

27. (previously presented) The method of organism disruption of claim 15 wherein the step of applying the surface acting agent includes applying more than one of a plurality of different surface acting agents.

28. (previously presented) The method of organism disruption of claim 15 wherein the step of passing the photosensitive material includes passing more than one of a plurality of different photosensitive materials.

29. (previously presented) The method of organism disruption of claim 15 wherein the step of applying a light includes a light wavelength ranging from 450 nm to 780 nm and a light dosage ranging from 10 J/cm^2 to 100 J/cm^2 and a light dosage rate ranging from 50 mw/cm^2 to 250 mw/cm^2.

30. (previously presented) The method of organism disruption of claim 15 wherein the organism is from a group containing: a virus, a spore, and a plasmid.

31. (previously presented) A method of photodynamic disruption of cells comprising the steps of:

identifying an area of cell activity;

applying a concentration including a combination of a benzalkonium chloride compound at a concentration of between 0.001% to 1.0% and a photosensitive material to the area of cell activity, said benzalkonium chloride compound disorienting a cell membrane so that said membrane no longer functions as an effective osmotic barrier, and so that said photosensitive material is able to pass through the disoriented cell membrane; and

exposing the area of cell activity to light having a light wavelength, a light dosage and a light dosage rate to cause photodynamic cellular disruption.

32. (previously presented) The method of photodynamic disruption of cells of claim 31 wherein the step of identifying an area of cell activity includes an examination and identification of a cell site on a living body, and the step of applying the concentration includes an application of the concentration to the cell site of the living body.

33. (original) The method of photodynamic disruption of cells of claim 31 wherein the step of identifying an area of cell activity includes identifying a medical prosthesis or device for sterilization procedure, and the step of providing the concentration includes an application of the concentration to a cell site of the prosthesis.

34. (original) The method of photodynamic disruption of cells of claim 31 wherein the step of identifying an area of cell activity includes identifying an air filtration/decontamination device, and the step of providing the concentration includes an application of the concentration to a cell site within the device.

35. (canceled)

36. (canceled)

37. (canceled)

38. (canceled)

39. (canceled)

40. (previously presented) A method of photodynamic eradication of organisms within a biofilm of a medical prosthesis, said method comprising the steps of:

applying a photosensitive material and a surfactant to a surface of the prosthesis supporting a biofilm;

allowing the surfactant to disrupt membranes of the organisms within the biofilm;

waiting a period of time until the photosensitive material accumulates within the organisms;

providing a source of light illumination having predetermined light characteristics; and

illuminating the organisms within the biofilm layer with the light source to achieve a photodynamic eradication of organisms within the biofilm layer.

41. (previously presented) The method of claim 40 wherein the surfactant is benzalkonium chloride provided in at a concentration of between 0.001% to 1.0%.

42. (previously presented) The method of claim 41 wherein the step of applying the photosensitive material and the surfactant is via an impregnation of compounds upon a surface of the prosthesis.

43. (original) The method of claim 41 wherein the step of illuminating the biofilm layer is achieved by an internal illumination of the prosthesis.

44. (original) The method of claim 41 wherein the step of illuminating the biofilm layer is achieved by an external light source illuminating the biofilm layer.

45. (previously presented) A method of photodynamic eradication of organisms within a biofilm layer of an endotracheal tube, said method comprising the steps of:

providing a photosensitive material and a surfactant to a surface of the endotracheal tube supporting a biofilm layer;

accumulating photosensitive material within the organisms comprising the biofilm;

allowing the surfactant to disrupt membranes of the organisms within the biofilm;

waiting a period of time until the photosensitive material accumulates within organisms;

providing a source of light illumination having predetermined light characteristics; and

illuminating the biofilm layer of the endotracheal tube with the light source to achieve a photodynamic eradication of organisms within the biofilm layer.

46. (previously presented) The method of claim 45 wherein the surfactant is benzalkonium chloride provided at a concentration of between 0.001% to 1.0%.

47. (original) The method of claim 45 wherein the step of providing the photosensitive material and the surfactant is via an impregnation of compounds upon a surface of the endotracheal tube.

48. (original) The method of claim 45 wherein the step of illuminating the biofilm layer is achieved by an internal illumination of the endotracheal tube.

49. (previously presented) A method of photodynamic eradication of organisms within a biofilm layer of an intravascular catheter, said method comprising the steps of:

providing a photosensitive material and a surfactant to a surface of the intravascular catheter supporting a biofilm layer;

accumulating photosensitive material within organisms comprising the biofilm;

allowing the surfactant to disrupt membranes of organisms within the biofilm;

waiting a period of time until the photosensitive material accumulates within the membranes of organisms within the biofilm;

providing a source of light illumination having predetermined light characteristics; and

illuminating the biofilm layer of the intravascular catheter with the light source to achieve a photodynamic eradication of organisms within the biofilm layer.

50. (previously presented) The method of claim 49 wherein the surfactant is benzalkonium chloride provided at a concentration of between 0.001% to 1.0%.

51. (original) The method of claim 49 wherein the step of providing the photosensitive material and the surfactant is via an impregnation of compounds upon a surface of the intravascular catheter.

52. (original) The method of claim 49 wherein the step of illuminating the biofilm layer is achieved by an internal illumination of the intravascular catheter.

EVIDENCE APPENDIX

Copies of the evidence submitted under 37 CFR 1.130, 1.131, or 1.132 or any other evidence entered by the examiner and relied upon by appellant in the appeal:

NONE

RELATED PROCEEDINGS APPENDIX

Decisions rendered by a court of the Board in the proceeding identified in the Related Appeals and Interferences section of the brief:

NONE